DOES ENVIRONMENTAL PERCHLORATE EXPOSURE ALTER HUMAN THYROID FUNCTION? DETERMINATION OF THE DOSE-RESPONSE FOR INHIBITION OF RADIOIODINE UPTAKE

M.A. Greer[1], G. Goodman[2], R.C. Pleus[3], S.E. Greer[1], [1]Oregon Health Sciences University 3181 SW Sam Jackson Park Road, Portland, OR, 97201, USA; [2]Human Health Risk Resources, Inc; [3]Intertox, Inc., Seattle, WA

The perchlorate ion (ClO_4^-) is a potent inhibitor of the sodium-iodide symporter. Over the past half-century, ClO_4^- at doses of 0.2 to 2 g/day has been utilized in the diagnosis and treatment of thyroid disease. ClO_4^- occurs in natural fertilizers and is manufactured for use as a propellant in rocket fuel. Recent improvement in analytical methods has led to widespread detection of ClO_4^- in drinking water, with most values <20 µg/L and almost all values <100 µg/L, yielding daily doses <0.6 and <3 µg/kg, respectively. As part of an effort to estimate the risk of thyroid hypofunction from environmental ClO_4^- exposure, we gave ClO_4^- at one of 3 doses to 24 euthyroid volunteers (4M and 4F per dose;18-57 yr-old) for 14 days. ClO_4^- was dissolved in drinking water to yield a daily dose of 0.02, 0.1, or 0.5 mg/kg (approx. 1.4, 7, or 35 mg assuming 70 kg body wt.) in 400 ml; subjects drank 100 ml at 4 set times throughout each day. Measurement of 8- and 24-hr ^{123}I thyroid uptakes was performed prior to ClO_4^- exposure (baseline), on exposure days 2 and 14, and on post-exposure day 15. Expressed as a percentage of baseline, mean (± SE) 24-hr uptakes in the 0.02, 0.1, and 0.5 mg/kg dose groups were 83 (5.6), 59 (3.5), 31 (2.6) on exposure day 2; 85 (4.5), 57 (4.7), 34 (4.5) on exposure day 14; and 111 (5.1), 96 (12), 108 (12) on post-exposure day 15. A linear log-dose relationship was observed. The 8-hr and 24-hr regression slopes were statistically indistinguishable. There was no M/F difference. Applied to exposure day 14, the 3-dose regression model predicts a no-effect dose (highest non-inhibitory dose) of 7 µg/kg (approx. 0.5 mg) per day. In 4 volunteers subsequently tested at this dose there was no inhibition of uptake, as predicted. The ED_{50} (50% effective dose) and maximum effective dose (lowest dose required to suppress uptake completely) are predicted by the 3-dose regression model to be 0.17 and 4.3 mg/kg (approx. 12 and 300 mg) per day, respectively. We are in the process of analyzing data on serum TT4, FT4, TT3, and TSH. Conclusions: We estimate that the no-effect dose of 0.5 mg/day would be consumed in drinking water containing ClO_4^- at 250 µg/L. Therefore, water supplies containing less than this should not affect human thyroid function.

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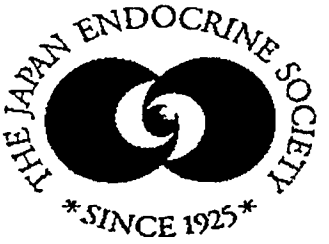

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